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| EXAMINER | |
|---|---|
| ROYDS, LESLIE A | |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTO.e-Office.rdg@boehringer-ingelheim.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/757,015 | RIEDEL ET AL. | |
| | Examiner | Art Unit | |
| | Leslie A. Royds | 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *09 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1 and 8-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 8-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

**Claims 1 and 8-35 are presented for examination.**

In view of the Appeal Brief filed on November 9, 2009, **PROSECUTION IS HEREBY REOPENED**. New grounds of rejection are set forth below.

To avoid abandonment of the application, Appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then Appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614

Claims 1 and 8-35 remain pending and under examination.

Applicant's arguments, presented in the Appeal Brief filed November 9, 2009, have been fully considered. Rejections and/or objections not reiterated from the final Office Action are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

***Claim Rejections - 35 USC § 112, First Paragraph, Scope of Enablement***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 8-17 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of asthma, bronchitis, interstitial lung disease, insulin resistance, prediabetes, type 2 diabetes mellitus, metabolic syndrome, hypertension combined with hyperlipidemia or hypertension combined with atherosclerosis comprising the administration of telmisartan (or a salt thereof) with simvastatin (or a salt thereof), does not reasonably provide enablement for the prevention of the same, for the reasons of record set forth at p.2-5 of the previous Office Action dated June 5, 2009, of which said reasons are herein incorporated by reference.

*Response to Applicant's Arguments*

Applicant traverses the instant rejection, stating that the grounds for rejection leave the impression that the claims are directed solely to prevention and are directed to providing an absolute cure to the conditions. Applicant further opines that the rejection is based upon the interpretation that the term "prevention" requires that the method would result in 0% occurrence of the condition and a guarantee that the condition would never develop. Applicant argues that this interpretation ignores that the claims recite "prevention or treatment". Applicant once again cites the decision rendered in *Ex parte Cho* in support of his position, stating that it "addresses the exact same issue on point here under non-distinguishing facts" and that the non-precedential nature of the opinion does not refute its clear logic. Applicant further opines that Grundy acknowledges the complexity of metabolic syndrome, but asserts that the fact that the condition may be complex does not support a lack of enablement when the condition is well understood in the art. Applicant argues that, given that the claimed method of treatment of metabolic syndrome is

admitted to be enabled, "it would follow that the method of prevention of metabolic syndrome would also be enabled regardless of the alleged "complex" nature of the syndrome" (p.6, Remarks). Applicant alleges that the specification provides extensive guidance as to how to prevent the claimed conditions by teaching that the combination(s) can be administered before patients are officially diagnosed and/or are suspected of having the claimed condition(s). Applicant cites to p.8-13 and 17-23 of the specification in support of his position that the disclosure provides guidance as to how to identify patients in need of the claimed method.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Firstly, Applicant argues that the grounds of rejection "leave the impression that the claims are directed solely to prevention". This is unpersuasive because the very basis for the rejection states that the claims, while being enabling for the treatment of the claimed diseases, are not adequately enabled for the prevention of the same claimed diseases. This clear acknowledgement refutes the allegation that the grounds for rejection only considers the claims to be directed solely to prevention, because it is explicitly stated on the record that the claims both circumscribe, *and are enabled for*, treating the claimed diseases.

Secondly, Applicant argues that the rejection is based upon the interpretation that the term "prevention" requires that the method would result in 0% occurrence of the condition and a guarantee that the condition would never develop, which Applicant opines ignores that the claims recite "prevention or treatment". This is unpersuasive because the rejection *does not*, contrary to Applicant's insistence, state that the term "prevention" requires 0% occurrence of the condition and a guarantee that the condition would never develop. Such an interpretation of the term "prevention" was not set forth in the grounds of the rejection. Therefore, Applicant's assertion that the rejection is based upon this interpretation of Counsel is clearly without merit because a full and complete consideration of the actual grounds of rejection clearly demonstrates that such an interpretation was not set forth as the basis of the rejection. Furthermore, the allegation that the rejection ignores the fact that the claims recite "prevention or

treatment" is also without merit because, once again, it is clearly and expressly set forth in the statement of the rejection that the claims, while being enabling for the treatment of the claimed diseases, are not adequately enabled for the prevention of the same claimed diseases. The fact that the claims have been analyzed to determine that they are adequately enabled insofar as they read upon the "treatment" of the instantly claimed diseases is clear evidence that the alternative language of "prevention or treatment" as recited in the instant claims has *not* been ignored.

Thirdly, Applicant again cites the decision rendered in *Ex parte Cho* in support of his position, stating that it "addresses the exact same issue on point here under non-distinguishing facts" and that the non-precedential nature of the opinion does not refute its clear logic. This is, and will remain, unpersuasive. The issue in *Cho* was that the Examiner had indicated a lack of enablement of various embodiments of the invention without providing an adequate explanation satisfying the initial burden of the examiner to show a lack of enablement. See p.7 of the *Cho* decision. This is *not*, contrary to Counsel's opinion, "the exact same issue on point here under non-distinguishing facts" because the present Examiner has provided, in the context of the instant rejection, extensive discussion as to why the claims lack enabling guidance for the full scope of the claims. Applicant's attention is directed to p.2-9 of the Office Action dated November 26, 2008 for these reasons. This instant conclusion of a lack of enablement *is not based upon unsupported assertions of a lack of enabling guidance*. Rather, the state of the prior art is clearly discussed in view of cited publications demonstrating the knowledge generally available in the art at the time of the invention taken in view of what is disclosed in the instant specification. Thus, the allegation that the "exact same issue" is addressed under "non-distinguishing facts" is a patent mischaracterization of the facts in the instant application as compared to the facts in the case under examination in *Cho*. Moreover, in view of these clearly distinguishing facts of the instant case and the case under discussion in *Cho*, Applicant continues to ignore the urging from the Office to explain why the decision has any relevance to the instant application *in view of the supporting evidence provided in the*

*instant rejection, as well as to provide a clear reason as to why the Office should be bound by a decision that is non-precedential in view of the clearly distinct fact patterns.*

Fourthly, Applicant opines that Grundy acknowledges the complexity of metabolic syndrome, but asserts that the fact that the condition may be complex does not support a lack of enablement when the condition is well understood in the art. This is, and will remain, unpersuasive. Not only does Grundy acknowledge the complexity of metabolic syndrome, he also expressly acknowledges that the art needs a better understanding of the link between insulin resistance and metabolic syndrome to provide improved management of the disease. See the abstract of Grundy, cited at p.5 of the Office Action dated November 26, 2008. Thus, while it may be true that the sheer complexity of a condition does not necessarily support a lack of enablement when the condition is well understood in the art, the fact remains that Grundy explicitly teaches that the condition *is not well understood in the art and, as such, a better and improved understanding is needed.* As a result, Applicant's position that the complexity of the condition does not support nonenablement when the condition is well understood is clearly faulty because the very teaching of Grundy is that the condition is *not* well understood in the art and, thus, the complexity and poor clinical understanding of the condition contributes to the lack of enabling guidance of the claimed embodiment directed to "prevention".

Fifthly, Applicant argues that, given that the claimed method of treatment of metabolic syndrome is admitted to be enabled, “it would follow that the method of prevention of metabolic syndrome would also be enabled regardless of the alleged 'complex' nature of the syndrome". This is unpersuasive because Applicant has failed to advance any reasons or evidence to support his position that the enablement of "preventing" metabolic syndrome can be inferred from the ability of the claimed combination to “treat” metabolic syndrome. Statements of this nature are unsupported allegations and are clearly unpersuasive in accordance with the guidance provided at MPEP §2145, which states, “The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA

1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ 2d 1362 (Fed. Cir. 1997)".

Sixthly, and lastly, Applicant alleges that the specification provides extensive guidance as to how to prevent the claimed conditions by teaching that the combination(s) can be administered before patients are officially diagnosed and/or are suspected of having the claimed condition(s) and cites to p.8-13 and 17-23 of the specification in support of his position that the disclosure provides guidance as to how to identify patients in need of the claimed method. This is unpersuasive. Though Applicant provides guidance as to what parameters may indicate disruption and/or predisposition to particular conditions, the instant specification still provides no guidance to one of ordinary skill in the art to show that the instantly claimed combination actually functions to *prevent* the development of the claimed disorders in such patients. Without such evidence, the state of the art at the time of the invention as evidenced by the publication to Grundy clearly demonstrates that the objective of prevention would not have been reasonably expected by one of skill in the art and the lack of enabling guidance fails to rebut the clear unpredictability in the art with regard to this same objective.

For these reasons *supra*, and those previously made of record at p.2-5 of the Office Action dated June 5, 2009, rejection of claims 1 and 8-17 is proper.

***Claim Rejections - 35 USC § 103 (New Grounds of Rejection)***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary.

Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 8-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over De Gasparo et al. (WO 01/76573; 2001), in light of Robl et al. (U.S. Patent Application Publication No. 2002/001334; January 31, 2002), which is cited to show a fact, in view of Wienen et al. ("A Review on Telmisartan: A Novel, Long-Acting Angiotensin II-Receptor Antagonist", *Cardiovascular Drug Reviews*, 18(2); 2000:127-154), Cecil's Textbook of Medicine (2000), Harlan et al. (U.S. Patent Application Publication No. 2001/0006656; July 2001) and Bohm et al. (WO 02/15892; February 2002).

De Gasparo et al. teaches a pharmaceutical composition (p.1, l.16) comprising an $AT_1$-receptor antagonist (p.1, l.27), or an $AT_1$-receptor antagonist in combination with a diuretic (p.1, l.27), or pharmaceutically acceptable salts thereof (p.1, l.28), further in combination with an HMG-CoA reductase inhibitor (p.1, l.29), and a carrier (p.2, l.1), used for the treatment of hyperlipidemia (p.1, l.8), atherosclerosis (p.1, l.8), insulin resistance (p.1, l.9), syndrome X (p.1, l.9), type 2 diabetes mellitus (p.1, l.9), renal failure (p.1, l.9-10), and all of these diseases of conditions associated with or without hypertension (p.1, l.12-13), in a warm-blooded animal, including man (p.2, l.4), wherein the therapeutically effective amount of $AT_1$-receptor antagonist given orally (given as a dosage of valsartan, which De Gasparo et al. expressly states is representative of the class of $AT_1$-receptor antagonists) is 20-320 mg (p.12, l.12-19) and the dose of HMG-CoA reductase inhibitor given orally is 5-120 mg (p.12, l.20-23). De Gasparo et al. expressly discloses telmisartan as the $AT_1$-receptor antagonist (p.3, l.22), simvastatin as the HMG-CoA reductase inhibitor (p.5, l.9-11) and hydrochlorothiazide and chlorothalidone as diuretic agents (p.4, l.8-10).

Robl et al. is relied upon to shown that Syndrome X is known to encompass prediabetic insulin

resistance syndrome (see paragraph [0107] at page 4), which is synonymous with prediabetes as required by Applicant's present claim 2.

De Gasparo et al. does not explicitly disclose (i) the preferable selection of telmisartan from the sartan compounds disclosed therein, (ii) that the human has the blood parameters of fasting blood sugar, triglycerides, HDL cholesterol or blood pressure (claims 9-13); (iii) the use of telmisartan and simvastatin for the treatment of asthma, bronchitis or interstitial lung disease (claim 1); or (iv) the particularly claimed dosage amounts of simvastatin, telmisartan or diuretic (i.e., hydrochlorothiazide or chlorothalidone) or weight ratio of simvastatin to telmisartan (claims 14-17, 21-26 and 33-35).

However, the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because:

(i) Wienen et al. teaches that telmisartan is a potent, long-lasting nonpeptide antagonist of the angiotensin II type-1 ($AT_1$) receptor that functions to inhibit stimulation of the $AT_1$ receptor by angiotensin II without affecting other receptor systems involved in cardiovascular regulation (abstract). Wienen et al. teaches that telmisartan has very high lipophilicity, which provides good tissue penetration, and has a longer terminal elimination half-life than other commercially available sartans, which makes it suitable for once-daily dosing (abstract). Wienen et al. further teaches that the compound is not metabolized by cytochrome P450 isoenzymes and has a low-risk for P450 based drug interactions, which demonstrates that telmisartan clearly offers advantages over other sartans (abstract).

One of ordinary skill in the art at the time of the invention would have found it *prima facie* obvious to select, specifically, telmisartan out of the genus of sartan compounds disclosed in De Gasparo et al. because, as evidenced by Wienen et al., telmisartan was known in the art at the time of the invention to provide significant advantages over other sartans due to its properties of inhibiting stimulation of the $AT_1$ receptor by angiotensin II without affecting other receptor systems involved in cardiovascular

regulation; very high lipophilicity, which corresponds to good tissue penetration; longer elimination half-life than other commercially available sartans, which reduces the frequency of dosing; and low frequency of drug interactions due to the fact that the compound is not metabolized by cytochrome P450. Such a person would have been motivated to make such a selection due to the many advantageous pharmacologic and therapeutic properties of telmisartan as compared to other similar sartan compounds, absent factual evidence to the contrary.

(ii) De Gasparo et al. expressly teaches hosts suffering from the presently claimed conditions (i.e., hypertension combined with hyperlipidemia or atherosclerosis, type 2 diabetes mellitus, prediabetes, metabolic syndrome, insulin resistance or hypertensive insulin resistance), but is silent as to the glucose, triglyceride or HDL cholesterol levels or blood pressure of the hosts contemplated by the reference. However, Cecil's Textbook of Medicine provides teachings of the standard, commonly accepted laboratory normal ranges for (1) normal serum glucose of 74-106 mg/dL, (2) normal serum triglyceride levels of <250 mg/dL; (3) normal HDL levels of >29 mg/dL for males and >35 mg/dL for females and (4) normal systolic blood pressure of <130 mmHg and normal diastolic blood pressure of <85 mmHg (see Cecil's, p.258 and 2299-2304). It would logically follow that the diabetic host of De Gasparo et al. would show elevated serum glucose outside of the normal range (i.e., greater than 110 mg/dL), the hyperlipidemic host would show elevated serum triglyceride levels on the outer limits of or outside the normal range (i.e., greater than 150 mg/dL) and low HDL cholesterol levels (i.e., <40 mg/dL for females and <50 mg/dL for males) and the hypertensive host would show elevated systolic and diastolic blood pressure (i.e., >130 mmHg systolic and >80 mmHg diastolic). While it is acknowledged that the reference standard ranges expressly taught by Cecil's are not exactly identical to those presently claimed, it must be noted that such serum levels of glucose, triglycerides, HDL cholesterol and blood pressure will vary by individual and, thus, what is considered "normal" or "abnormal" will also vary such that a proper comparison to determine whether a particular laboratory value is normal or abnormal must be made to

baseline values for each patient. Regardless of the minor differences between Cecil's and the present claims, the presently claimed limitations on the diabetic, hyperlipidemic or hypertensive host by claiming particular serum levels of glucose, triglycerides, HDL cholesterol or blood pressure are not considered to impart patentable distinction to the present claims over what would have been logically determined from the teachings of De Gasparo et al. in light of the knowledge generally available to one of ordinary skill in the art at the time of the invention.

(iii) Harlan et al. provides teachings of the use of an HMG-CoA reductase inhibitor, such as simvastatin, for the treatment of inflammatory lung diseases, such as asthma, chronic bronchitis and interstitial lung disease (see para.[0022] and [0025-0026] at p.2). Although Harlan et al. is silent as to the concomitant use of an angiotensin antagonist, such as telmisartan, for the treatment of the same, Bohm et al. teaches that diseases such as bronchitis, asthma and interstitial lung disease were known to be associated with an increase of $AT_1$ receptors in the subepithelial area and, thus, were amenable to treatment using a composition comprising an $AT_1$ antagonist, such as telmisartan (p.7, para.6-7 and p.10, para.2).

While De Gasparo et al. is silent as to the particular treatment of asthma, bronchitis or interstitial lung disease, the teachings of Harlan et al. and Bohm et al. raise the reasonable expectation of success that an $AT_1$ antagonist, such as telmisartan, and an HMG-CoA reductase inhibitor, such as simvastatin, would demonstrate efficacy in the treatment of asthma, bronchitis or interstitial lung disease when combined, since each was known to be used separately in the art for the same indication(s). Motivation to administer both compounds flows logically from the efficacy of each compound in treating asthma, bronchitis or interstitial lung disease. One having ordinary skill in the art would have been motivated to administer simvastatin and telmisartan together for the treatment of the same because each compound has been previously administered for these identical therapeutic endpoints and would have been reasonably expected to achieve, at minimum, additive, if not synergistic, effects when combined. In the absence of

evidence to the contrary, it is generally *prima facie* obvious to use in combination two or more agents that have previously been used separately for the same purpose. Please see *In re Kerkhoven*, 626 F.2d 846, 205 USPQ 1069, at page 1072 (CCPA 1980) ["It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose. *In re Susi*, 58 CCPA 1074, 1079-80, 440 F.2d 442, 445, 169 USPQ 423, 426 (1971); *In re Crockett*, 47 CCPA 1018, 1020-21, 279 F.2d 274, 276-77, 126 USPQ 186, 188 (CCPA 1960)."] and *In re Diamond and Kellman*, 149 USPQ 562 (CCPA 1966).

(iii) The determination of the optimum amounts or weight ratio(s) of simvastatin and telmisartan to treat the presently claimed diseases (i.e., hypertension combined with hyperlipidemia or atherosclerosis, diabetes mellitus, prediabetes, metabolic syndrome, insulin resistance or hypertensive insulin resistance) with the presently claimed active agents would have been a matter well within the purview of one of ordinary skill in the art. Such a determination would have been made in accordance with a variety of factors, such as the age, weight, sex, diet and medical condition of the patient, severity of the disease, the route of administration, pharmacological considerations, such as the activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus, the amounts or ratios that would have actually been employed would have varied widely and, in the absence of evidence to the contrary, the currently claimed specific amounts or weight ratio(s) are not seen to be inconsistent with those that would have been determined by the skilled artisan. Furthermore, absent any evidence demonstrating a patentable difference between the compositions and the criticality of the claimed amounts, the determination of the optimum or workable range(s) given the guidance of the prior art would have been generally *prima facie* obvious to the skilled artisan. Please see MPEP §2144.05[R-2](II)(A) and *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) ("[W]here the general conditions of claim are disclosed in the prior art, it is not inventive to discover the optimum or workable

ranges by routine experimentation.").

***Double Patenting (New Grounds of Rejection)***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 8-35 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 2 and 7-18 of U.S. Patent Application No. 10/757,295, in view of Harlan et al. (U.S. Patent Application Publication No. 2001/0006656; 2001).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims because the examined claims is either anticipated by, or would have been obvious over, the reference claims.

Although the conflicting claims are not identical, the claims of the present application and those of the copending patent application are not considered patentably distinct from each other because the copending claims render the present claims obvious.

The copending claims clearly provide for the treatment of hypertension combined with hyperlipidemia or atherosclerosis, asthma, bronchitis, interstitial lung disease, diabetes mellitus, prediabetes, metabolic syndrome, insulin resistance or hypertensive insulin resistance in a human or mammalian host comprising the administration of telmisartan with atorvastatin. While the present claims are drawn to the same therapeutic objectives, the present claims recite the administration of telmisartan

with simvastatin. However, the use of simvastatin instead of atorvastatin would have been *prima facie* obvious to one of ordinary skill in the art since simvastatin was known in the art to have the same functionality as an HMG-CoA reductase inhibitor as atorvastatin (see Harlan et al., para.[0025] at p.2) and would have been reasonably expected to be functional equivalents and, thus, would have been understood to be interchangeable as a result of their substantially similar efficacy as HMG-CoA reductase inhibitors.

Furthermore, the copending claims are also drawn to a pharmaceutical composition comprising telmisartan, atorvastatin, a carrier and, optionally, a diuretic, which is identical to the composition of the present claims, but for the use of atorvastatin instead of simvastatin. As previously stated, simvastatin was known in the art to have the same functionality as having an inhibitory effect on HMG-CoA reductase as atorvastatin and would have been reasonably expected to be functional equivalents and, thus, would have been understood to be interchangeable as a result of their substantially similar efficacy as HMG-CoA reductase inhibitors.

Lastly, while the dosage amounts or concentrations of the active agents to be administered or contained in the composition are not identical between the present claims and the copending claims, it is noted that the determination of the optimum dosage regimen or amounts would have been well within the purview of the skilled artisan and would have been made in accordance with a variety of factors, including, but not limited to, the age, sex, weight, diet, and medical condition of the patient, toxicological considerations and the severity of the disease.

Accordingly, rejection of claims 1 and 8-35 of the present application is deemed proper over claims 2 and 7-18 of U.S. Patent Application No. 10/757,295 as claiming obvious and unpatentable variants thereof. This is a provisional double patenting rejection since the conflicting claims of this application have not yet been patented.

Claims 18-35 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claim 18 of U.S. Patent Application No. 10/899,784 in view of De Gasparo et al. (WO 01/76573; 2001).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims because the examined claims is either anticipated by, or would have been obvious over, the reference claims.

Although the conflicting claims are not identical, the claims of the present application and those of the copending patent application are not considered patentably distinct from each other because the copending claims render the present claims obvious.

The copending claim provides for a pharmaceutical composition containing a pharmaceutically effective amount of telmisartan in conjunction with a pharmaceutically effective amount of, *inter alia*, simvastatin.

The copending claims fail to teach the incorporation of a diuretic, such as hydrochlorothiazide with chlorothalidone (claims 27-35) or the specific amounts of the active agents (claims 21-26 and 33-35).

De Gasparo et al. teaches a pharmaceutical composition (p.1, l.16) comprising an $AT_1$-receptor antagonist or an $AT_1$-receptor antagonist in combination with a diuretic (p.1, l.27), or pharmaceutically acceptable salts thereof (p.1, l.28), further in combination with an HMG-CoA reductase inhibitor (p.1, l.29), and a carrier (p.2, l.1), used for the treatment of hyperlipidemia (p.1, l.8), atherosclerosis (p.1, l.8), insulin resistance (p.1, l.9), syndrome X (p.1, l.9), type 2 diabetes mellitus (p.1, l.9), renal failure (p.1, l.9-10), and all of these diseases of conditions associated with or without hypertension (p.1, l.12-13), in a warm-blooded animal, including man (p.2, l.4), wherein the therapeutically effective amount of $AT_1$-receptor antagonist given orally (given as a dosage of valsartan, which De Gasparo et al. expressly states

is representative of the class of $AT_1$-receptor antagonists) is 20-320 mg (p.12, l.12-19) and the dose of HMG-CoA reductase inhibitor given orally is 5-120 mg (p.12, l.20-23). De Gasparo et al. expressly discloses telmisartan as the $AT_1$-receptor antagonist (p.3, l.22), simvastatin as the HMG-CoA reductase inhibitor (p.5, l.9-11) and hydrochlorothiazide and chlorthalidone as diuretic agents (p.4, l.8-10).

One of ordinary skill in the art at the time of the invention would have found it *prima facie* obvious to incorporate a diuretic compound, such as hydrochlorothiazide or chlorothalidone, into the telmisartan composition of the copending claims because, as evidenced by De Gasparo et al., a composition comprising an $AT_1$ antagonist (such as telmisartan) and an HMG-CoA reductase inhibitor (such as simvastatin) were known to be effective for the treatment of the same conditions as an $AT_1$ antagonist (such as telmisartan) and an HMG-CoA reductase inhibitor (such as simvastatin) and a diuretic (such as hydrochlorothiazide or chlorothalidone), wherein each combination was known to be effective for the treatment of hyperlipidemia, atherosclerosis, insulin resistance, syndrome X, type 2 diabetes mellitus, renal failure, and all of these diseases of conditions associated with or without hypertension, in humans. The desirability of including administering a diuretic in combination with the $AT_1$ antagonist and HMG-CoA reductase inhibitor combination flows logically from the efficacy of each combination for treating hyperlipidemia, etc. One having ordinary skill in the art would have been motivated to administer a diuretic compound in combination with the telmisartan composition of the copending claims because each combination was known to be effective for identical therapeutic endpoints and would have been reasonably expected to achieve, at minimum, additive, if not synergistic, effects when combined. In the absence of evidence to the contrary, it is generally *prima facie* obvious to use in combination two or more agents that have previously been used separately for the same purpose. Please see *In re Kerkhoven*, 626 F.2d 846, 205 USPQ 1069, at page 1072 (CCPA 1980) ["It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose. *In re Susi*, 58 CCPA 1074, 1079-80,

440 F.2d 442, 445, 169 USPQ 423, 426 (1971); *In re Crockett*, 47 CCPA 1018, 1020-21, 279 F.2d 274, 276-77, 126 USPQ 186, 188 (CCPA 1960)."] and *In re Diamond and Kellman*, 149 USPQ 562 (CCPA 1966).

Lastly, while the dosage amounts or concentrations of the active agents to be administered or contained in the composition are not identical between the present claims and the copending claims, it is noted that the determination of the optimum dosage regimen or amounts would have been well within the purview of the skilled artisan and would have been made in accordance with a variety of factors, including, but not limited to, the age, sex, weight, diet, and medical condition of the patient, toxicological considerations and the severity of the disease.

Accordingly, rejection of claims 18-35 of the present application is deemed proper over claim 18 of U.S. Patent Application No. 10/899,784 as claiming obvious and unpatentable variants thereof. This is a provisional double patenting rejection since the conflicting claims of this application have not yet been patented.

Claims 18-35 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-17 and 22 of U.S. Patent Application No. 11/300,947 in view of De Gasparo et al. (WO 01/76573; 2001).

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claims because the examined claims is either anticipated by, or would have been obvious over, the reference claims.

Although the conflicting claims are not identical, the claims of the present application and those of the copending patent application are not considered patentably distinct from each other because the copending claims render the present claims obvious.

The copending claims provide for a pharmaceutical composition comprising about 160 mg of telmisartan or a salt thereof and about 50 mg of hydrochlorothiazide, wherein the composition may further comprising other excipients and adjuvants.

The copending claims fail to teach the incorporation of an HMG-CoA reductase inhibitor, such as simvastatin (claims 18-35), or the specific amounts of the active agents (claims 21-26 and 33-35).

De Gasparo et al. teaches a pharmaceutical composition (p.1, l.16) comprising an $AT_1$-receptor antagonist or an $AT_1$-receptor antagonist in combination with a diuretic (p.1, l.27), or pharmaceutically acceptable salts thereof (p.1, l.28), further in combination with an HMG-CoA reductase inhibitor (p.1, l.29), and a carrier (p.2, l.1), used for the treatment of hyperlipidemia (p.1, l.8), atherosclerosis (p.1, l.8), insulin resistance (p.1, l.9), syndrome X (p.1, l.9), type 2 diabetes mellitus (p.1, l.9), renal failure (p.1, l.9-10), and all of these diseases of conditions associated with or without hypertension (p.1, l.12-13), in a warm-blooded animal, including man (p.2, l.4), wherein the therapeutically effective amount of $AT_1$-receptor antagonist given orally (given as a dosage of valsartan, which De Gasparo et al. expressly states is representative of the class of $AT_1$-receptor antagonists) is 20-320 mg (p.12, l.12-19) and the dose of HMG-CoA reductase inhibitor given orally is 5-120 mg (p.12, l.20-23). De Gasparo et al. expressly discloses telmisartan as the $AT_1$-receptor antagonist (p.3, l.22), simvastatin as the HMG-CoA reductase inhibitor (p.5, l.9-11) and hydrochlorothiazide and chlorthalidone as diuretic agents (p.4, l.8-10).

One of ordinary skill in the art at the time of the invention would have found it *prima facie* obvious to incorporate an HMG-CoA reductase inhibitor, such as simvastatin, into the telmisartan composition of the copending claims because, as evidenced by De Gasparo et al., a composition comprising an $AT_1$ antagonist (such as telmisartan) and a diuretic (such as hydrochlorothiazide or chlorthalidone) was known to be effective for the treatment of the same conditions as an $AT_1$ antagonist (such as telmisartan) and an HMG-CoA reductase inhibitor (such as simvastatin) and a diuretic (such as hydrochlorothiazide or chlorothalidone), wherein each combination was known to be effective for the

treatment of hyperlipidemia, atherosclerosis, insulin resistance, syndrome X, type 2 diabetes mellitus, renal failure, and all of these diseases of conditions associated with or without hypertension, in humans. The desirability of including administering an HMG-CoA reductase inhibitor in combination with the $AT_1$ antagonist and diuretic combination flows logically from the efficacy of each combination for treating hyperlipidemia, etc. One having ordinary skill in the art would have been motivated to administer an HMG-CoA reductase inhibitor compound in combination with the telmisartan composition of the copending claims because each combination was known to be effective for identical therapeutic endpoints and would have been reasonably expected to achieve, at minimum, additive, if not synergistic, effects when combined. In the absence of evidence to the contrary, it is generally *prima facie* obvious to use in combination two or more agents that have previously been used separately for the same purpose. Please see *In re Kerkhoven*, 626 F.2d 846, 205 USPQ 1069, at page 1072 (CCPA 1980) ["It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose. *In re Susi*, 58 CCPA 1074, 1079-80, 440 F.2d 442, 445, 169 USPQ 423, 426 (1971); *In re Crockett*, 47 CCPA 1018, 1020-21, 279 F.2d 274, 276-77, 126 USPQ 186, 188 (CCPA 1960)."] and *In re Diamond and Kellman*, 149 USPQ 562 (CCPA 1966).

Lastly, while the dosage amounts or concentrations of the active agents to be administered or contained in the composition are not identical between the present claims and the copending claims, it is noted that the determination of the optimum dosage regimen or amounts would have been well within the purview of the skilled artisan and would have been made in accordance with a variety of factors, including, but not limited to, the age, sex, weight, diet, and medical condition of the patient, toxicological considerations and the severity of the disease.

Accordingly, rejection of claims 18-35 of the present application is deemed proper over claim 1-17 and 22 of U.S. Patent Application No. 11/300,947 as claiming obvious and unpatentable variants

thereof. This is a provisional double patenting rejection since the conflicting claims of this application have not yet been patented.

***Conclusion***

Rejection of claims 1 and 8-35 is proper.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/
Primary Examiner, Art Unit 1614

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